Claim Rejections - 35 U.S.C. § 101

Claims 23-29 are rejected by the examiner under 35 U.S.C. § 101 for allegedly not being supported by a specific and substantial asserted utility. Applicant respectfully traverses and requests reconsideration and withdrawal of the rejection.

The examiner defines "specific utility" as a utility that is specific to the subject matter claimed. The examiner defines "substantial utility" as a "real world" use. Applicant asserts that the presently claimed method of identifying compounds that modulate the function of C-RET receptor protein kinase is supported by a specific and substantial utility. Several human diseases have been linked to mutations in the RET proto-oncogene. Multiple endocrine neoplasia types 2A and 2B (MEN2A and MEN2B) and medullary thyroid carcinoma are associated with germline mutations of the RET proto-oncogene. See Santoro, M., et al., *Science*, **267**, (1995) 381-383 (Appendix I). Santoro et al. reports that oncogenic conversion of RET in these neoplastic syndromes establishes germline transmission of dominant transforming genes in human cancer. Takahashi also discloses diseases that are caused by RET mutations, such as MEN2A, MEN2B, papillary thyroid carcinoma and Hirschsprung's. Additionally, on page 27 of applicant's own specification, Hirschsprung's disease is listed as a disease that is associated with C-RET mutations. As well, on page 27 of the specification, it indicates that over-expression of RET in cells is implicated in cancers, such as cancer of the thyroid. Therefore, since mutations in the RET proto-oncogene have been linked to several human diseases, the claimed method of identifying compounds that modulate the function of C-RET receptor protein kinase possesses a specific and substantial utility.

Moreover, as shown in column 5, lines 42-48 of U.S. Patent No. 6,235,769 (Appendix A); page 362 of Takahashi, M., *Cytokine and Growth Factor Reviews* **12** (2001) 361-373, page 362 (Appendix B); and page 4 of http://www.intouchlive.com/cancergenetics/onco.htm (Appendix C), C-RET is a proto-oncogene. A proto-oncogene, as defined by The Dictionary of Cell and Molecular Biology is "[t]he normal, cellular equivalent of an oncogene; thus usually a gene involved in the signaling or regulation of cell growth. In general, cellular proto-oncogenes are prefixed with a 'c', rather than their abnormal viral counterparts, that are

prefixed with a 'v', eg. c-myc and v-myc." See Appendix D. An oncogene, as defined by The Dictionary of Cell and Molecular Biology is a "[m]utated and/or overexpressed version of a normal gene of animal cells (the proto-oncogene) that in a dominant fashion can release the cell from normal restraints on growth, and thus alone, or in concert with other changes, convert a cell into a tumor cell." See Appendix E. Therefore, since C-RET has been categorized as a proto-oncogene, the skilled artisan would know that a utility for the claimed method is to identify compounds that can be used to prevent tumor development.

Finally, with respect to the examiner's assertion on page 4 of the outstanding Office Action that there is no showing that GDNF promotes the survival and phenotype of central dopaminergic, noradrenergic and motor neurons via its interaction with C-RET, applicant directs the examiner's attention to Durbec, P., et al. *Nature* **381** (1996) 789-792. See Appendix F. Durbec et al. studied many aspects of the interaction between RET and GDNF, including the effect on neuronal response, and concluded that their data "strongly suggests that the C-RET locus encodes a functional receptor for GDNF." See page 791. Additionally, Buj-Bello, A., et al., *Nature* **387** (1997) 721-724 (Appendix G) showed that GDNF promotes neuronal survival by signaling through a multicomponent receptor that consists of RET and a member of a GPI-linked family of receptors that determines ligand specificity. See abstract. See also Gratacos, E., et al., *Journal of Neurochemistry* **78** (2001) 1287-1296 (Appendix H).

Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claims 23-29 are rejected by the examiner under 35 U.S.C. § 112, first paragraph, for lack of enablement. Applicant respectfully traverses and request reconsideration and withdrawal of the rejection.

The examiner asserts that since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skill in the art would not know how to use the claimed invention. As discussed above, the present invention is supported by both a specific and substantial asserted utility and a well established utility. Therefore, a person of skill in the art would know how to use the claimed invention. Thus, the present claims comply with the requirements of 35 U.S.C. § 112, first paragraph.

CONCLUSION

As the above-presented amendments and remarks address and overcome all of the rejections presented by the Examiner, withdrawal of the rejections and allowance of the claims are respectfully requested.

If the Examiner has any questions concerning this application, he or she is requested to contact the undersigned.

Respectfully submitted,

Date January 14, 2002

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.